



The Naples Score: Can it Outperform Existing Scores in Predicting Gastric Cancer Mortality?

Naples Skoru: Mide Kanseri Ölümlerini Tahmin Etmede Mevcut Skorlardan Daha İyi Performans Gösterebilir mi?

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ABSTRACT

Objective: Gastric cancer surgery, including curative and palliative procedures, is crucial for managing gastric cancer. Accurate assessment of nutritional status is essential for risk stratification and improving patient outcomes. This retrospective study aims to identify the most reliable predictors of postoperative mortality by investigating the correlation between four nutritional scores and the mortality rate following gastric cancer surgery.

Material and Method: This retrospective study evaluated 50 patients diagnosed with gastric adenocarcinoma and operated on at Hitit University Department of General Surgery between April 2021 and September 2023. Nutritional scores were calculated using albumin, cholesterol, neutrophil-to-lymphocyte ratio, and lymphocyte-to-monocyte ratio, along with mortality rates. Data collected included age, gender, operation type, laparoscopy usage, albumin, cholesterol, neutrophil-to-lymphocyte ratio, lymphocyte-to-monocyte ratio, mortality rates, and TNM stages. Nutritional scores were calculated, and their predictive accuracy for mortality was assessed using time-dependent Receiver Operating Characteristic curve analysis.

Results: Significant differences in albumin levels, neutrophil-to-lymphocyte ratio, lymphocyte-to-monocyte ratio, and nutritional scores were found between deceased and surviving patients. Specifically, albumin levels were significantly lower in deceased patients (median = 3.5 mg/dL) compared to surviving patients (median = 4.1 mg/dL, $p=0.001$). The median neutrophil-to-lymphocyte ratio was higher in deceased patients ($p=0.005$), and the median lymphocyte-to-monocyte ratio was lower in deceased patients ($p=0.009$). Among the scores, the Naples Prognostic Score was significantly associated with mortality but was outperformed by the Prognostic Nutritional Index. The Prognostic Nutritional Index had the highest predictive accuracy with an Area Under the curve of 0.792, a sensitivity of 76%, and a specificity of 86.2%, outperforming the others.

Conclusion: Among the evaluated scores, the Prognostic Nutritional Index is the most effective predictor of prognosis. Its superior predictive accuracy suggests that the PNI can be utilized to enhance risk assessment and guide nutritional interventions in gastric cancer patients undergoing surgery.

Keywords: Gastric cancer, mortality, predictor.

ÖZET

Amaç: Küratif ve palyatif prosedürler dahil olmak üzere mide kanseri cerrahisi, mide kanserinin yönetiminde çok önemlidir. Beslenme durumunun doğru değerlendirilmesi, risk sınıflandırması ve hasta sonuçlarının iyileştirilmesi için esastır. Bu retrospektif çalışma, dört beslenme skoru ile mide kanseri cerrahisi sonrası mortalite oranı arasındaki ilişkiyi inceleyerek postoperatif mortalitenin en güvenilir öngörücülerini belirlemeyi amaçlamaktadır.

Gereç ve Yöntem: Bu retrospektif çalışma, Nisan 2021 ile Eylül 2023 arasında Hitit Üniversitesi Genel Cerrahi Kliniğinde ameliyat edilen mide adenokarsinomu tanısı konulan 50 hastayı değerlendirdi. Beslenme skorları, albümin, kolesterol, nötrofil-lenfosit oranı, lenfosit-monosit oranı ve mortalite oranları kullanılarak hesaplandı. Toplanan veriler arasında yaş, cinsiyet, operasyon tipi, laparoskopik kullanımı, albümin, kolesterol, nötrofil-lenfosit oranı, lenfosit-monosit oranı, mortalite oranları ve TNM evreleri yer aldı. Beslenme skorları hesaplandı ve mortaliteyi öngörmedeki doğrulukları zaman bağımlı Alıcı İşletim Karakteristik eğrisi analizi kullanılarak değerlendirildi.

Bulgular: Albümin seviyeleri, nötrofil-lenfosit oranı, lenfosit-monosit oranı ve beslenme skorları arasında ölen ve hayatta kalan hastalar arasında anlamlı farklılıklar bulundu. Özellikle, albümin seviyeleri ölen hastalarda (medyan = 3,5 mg/dL) hayatta kalan hastalara kıyasla (medyan = 4,1 mg/dL, $p=0,001$) anlamlı derecede daha düşüktü. Ölen hastalarda medyan nötrofil-lenfosit oranı daha yüksekti ($p=0,005$) ve medyan lenfosit-monosit oranı daha düşüktü ($p=0,009$). Skorlar arasında, Naples Prognostic Skoru mortalite ile anlamlı derecede ilişkiliydi ancak Prognostic Nutritional Index tarafından aşıldı. Prognostic Nutritional Index, 0,792'lik bir eğri altındaki alan, %76 duyarlılık ve %86,2 özgüllük ile en yüksek öngörü doğruluğuna sahipti ve diğerlerini geride bıraktı.

Sonuç: Değerlendirilen skorlar arasında, Prognostic Nutritional Index prognozun en etkili öngörücüsüdür. Üstün öngörü doğruluğu, PNI'nin mide kanseri cerrahisi geçiren hastalarda risk değerlendirmesini geliştirmek ve beslenme müdahalelerini yönlendirmek için kullanılabileceğini önermektedir.

Anahtar Sözcükler: Mide kanseri, mortalite, öngörücü.

Introduction

Gastric cancer surgery, particularly curative procedures, remains a cornerstone in the management of gastric cancer (GC). According to established guidelines, palliative resections generally do not contribute to survival benefits except in emergency cases. GC ranks among the leading causes of cancer-related deaths worldwide. The prognosis is particularly poor in metastatic patients. The nutritional status of these patients is often worse due to gastrointestinal involvement and cancer-related cachexia. Impaired nutritional status and immune response are among the reasons for the short survival time in these patients (1). Despite advances in surgical techniques and perioperative care, postoperative mortality continues to be a significant concern, with rates varying based on a multitude of factors including patient nutritional status. Malnutrition, often observed in patients undergoing gastric cancer surgery, has been implicated in increased postoperative complications and mortality. Therefore, accurate assessment of nutritional status is crucial for risk stratification and improving patient outcomes (2).

Several nutritional scoring systems have been developed to evaluate the nutritional status and predict outcomes in surgical patients (3). Among these, the Naples Prognostic Score (NPS), Controlling Nutritional Status (CONUT) score, Prognostic Nutritional Index (PNI), and Systemic Inflammation Score (SIS) are widely recognized (4,5). Each of these scores integrates various biochemical and clinical parameters to provide a comprehensive assessment of a patient's nutritional and inflammatory status. The NPS incorporates albumin levels, total cholesterol, lymphocyte count, and neutrophil-to-lymphocyte ratio, reflecting both nutritional and systemic inflammatory conditions. The CONUT score, derived from serum albumin, total cholesterol, and lymphocyte count, similarly provides an indication of protein reserves, caloric depletion, and immune competence. The PNI, calculated using serum albumin concentration and total lymphocyte count, is another established predictor of surgical outcomes and overall prognosis. Lastly, the SIS combines the albumin level with the lymphocyte-to-monocyte ratio, emphasizing the role of systemic inflammation in patient prognosis. The Naples Prognostic Score (NPS) incorporates

albumin levels, total cholesterol, lymphocyte count, and neutrophil-to-lymphocyte ratio, reflecting both nutritional and systemic inflammatory conditions (6). The CONUT score, derived from serum albumin, total cholesterol, and lymphocyte count, similarly provides an indication of protein reserves, caloric depletion, and immune competence (7). The Prognostic Nutritional Index (PNI), calculated using serum albumin concentration and total lymphocyte count, is another established predictor of surgical outcomes and overall prognosis (8). Lastly, the Systemic Inflammation Score (SIS) combines the albumin level with the lymphocyte-to-monocyte ratio, emphasizing the role of systemic inflammation in patient prognosis (9).

Previous studies have demonstrated the utility of these scores in various clinical settings, yet their comparative effectiveness in predicting prognosis specifically in gastric cancer patients remains underexplored (10). Understanding the relative predictive value of these scores can guide clinical decision-making and optimize perioperative care strategies.

This study aims to investigate the correlation between these four nutritional scores and the mortality rate following gastric cancer surgery. By evaluating the predictive accuracy of NPS, CONUT, PNI, and SIS, we seek to identify the most reliable predictors of prognosis, thereby facilitating better risk assessment and targeted nutritional interventions for patients undergoing gastric cancer surgery.

Material and Methods

This retrospective study evaluated 50 patients diagnosed with gastric adenocarcinoma and operated on at a single center between April 2021 and September 2023. Individuals under the age of 18 and above the age of 80, those with known hematological and oncological diseases, those with known vascular and endothelial diseases, and those whose data could not be accessed were excluded from the study. A total of 50 patients were included in the study after applying the exclusion criteria. Data collected included age, gender, operation type, laparoscopy usage, albumin, cholesterol, neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), mortality rates, Naples

score, CONUT score, PNI score, SIS score, and TNM stages. Survival analysis was performed to provide a more accurate assessment of patient outcomes. This study received ethical approval from the local ethics committee institutional review board (Protocol Number: 2023/178).

Statistical analyses were conducted using IBM SPSS Statistics for Windows software (version 26; IBM Corp., Armonk, N.Y., USA). Descriptive statistics were reported for categorical variables as counts and percentages, and for numerical variables as mean \pm standard deviation for normally distributed variables and median (minimum-maximum) values for non-Gaussian distributed variables. The normal distribution of data was assessed using the Shapiro-Wilk test. Correlations between variables were evaluated using Pearson and Spearman correlation coefficients, depending on the data distribution. Comparison of numerical measurements between independent groups, such as age, cholesterol levels, and PNI, was assessed using the Student's t-test, while non-Gaussian distributed variables were assessed with the Mann-Whitney U test, considering the distribution of the data. Categorical variables such as gender, operation type, laparoscopy usage, mortality rate, Naples groups, and TNM stages were evaluated between research groups using the Chi-square test. Survival analysis was conducted using the Kaplan-Meier method, and the differences between groups were compared using the log-rank test. Cox regression analysis was employed for multivariate analysis of the parameters to determine their impact on survival. Receiver Operating Characteristic (ROC) curves were utilized to demonstrate the discriminative ability of nutritional scores. Cut-off values for these markers were determined using the area under the curve and the Youden index. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy values were calculated based on these cut-off values. Odds ratio values were computed for these cut-off points. A significance level of $p < 0.05$ was considered statistically significant.

Results

A total of 50 patients met the inclusion criteria for the study. The mean age of the patients was 65.58 ± 10.67 years. Eighty percent of the patients

were male. Sixty-six percent of the patients had undergone total gastrectomy, and thirty-four percent had undergone subtotal gastrectomy. Laparoscopy was used in forty-six percent of surgeries. Twenty-one patients had died during the follow-up period since undergoing the procedure.

Table I Demographic specifications of the patients and comparison between the patient groups

Variables	All Patients (n=50)	Alive (n=29)	Deceased (n=21)	p	
Age	65.58 \pm 10.67	64.28 \pm 10.64	67.38 \pm 10.7	0.375	
Gender	Male	40 (80%)	25 (86.21%)	15 (71.43%)	0.286
	Female	10 (20%)	4 (13.79%)	6 (28.57%)	
Operation Type	Subtotal	17 (34%)	9 (31.03%)	8 (38.1%)	0.603
	Total	33 (66%)	20 (68.97%)	13 (61.9%)	
Laparoscopic	Laparotomy	27 (54%)	15 (51.72%)	12 (57.14%)	0.704
	Laparoscopy	23 (46%)	14 (48.28%)	9 (42.86%)	
Albumin	3.95 (2.6-4.5)	4.1 (3.2-4.4)	3.5 (2.6-4.5)	0.001	
Cholesterol	174.8 \pm 45.1	181.14 \pm 39.46	166.14 \pm 51.63	0.250	
NLR	3.06 (1.27-109.6)	2.55 (1.27-6.51)	3.95 (1.77-109.6)	0.005	
LMR	3.04 (1.26-7.36)	3.22 (1.27-7.36)	2.27 (1.26-4.5)	0.009	
Naples Group	Naples Score 0	3 (6%)	2 (6.9%)	1 (4.76%)	0.022
	Naples Score 1-2	25 (50%)	19 (65.52%)	6 (28.57%)	
	Naples Score 3-4	22 (44%)	8 (27.59%)	14 (66.67%)	
CONUT	2 (0-10)	2 (0-5)	4 (0-10)	0.004	
PNI	46.13 \pm 6.93	49.06 \pm 5	42.08 \pm 7.29	<0.001	
SIS	1 (0-2)	1 (0-2)	2 (0-2)	<0.001	
TNM	T1N0	9 (18%)	9 (31.03%)	0 (0%)	0.053
	T2N0	1 (2%)	1 (3.45%)	0 (0%)	
	T2N1	1 (2%)	0 (0%)	1 (4.76%)	
	T3N0	6 (12%)	5 (17.24%)	1 (4.76%)	
	T3N1	3 (6%)	0 (0%)	3 (14.29%)	
	T3N2	3 (6%)	2 (6.9%)	1 (4.76%)	
	T3N3	10 (20%)	3 (10.34%)	7 (33.33%)	
	T4N0	2 (4%)	1 (3.45%)	1 (4.76%)	
	T4N1	2 (4%)	1 (3.45%)	1 (4.76%)	
	T4N2	3 (6%)	2 (6.9%)	1 (4.76%)	
	T4N3	10 (20%)	5 (17.24%)	5 (23.81%)	

NLR: Neutrophil-to-Lymphocyte Ratio, LMR: Lymphocyte-to-Monocyte Ratio, CONUT: Controlling Nutritional Status, PNI: Prognostic Nutritional Index, SIS: Systemic Inflammation Score Shapiro-Wilks test, Student t-test, Mann Whitney-U test, Chi-square test

When the subjects were divided into two groups based on mortality status, no statistically significant

Table II Optimal cut-off values for the distinction between alive and deceased groups and diagnostic indicators (Youden index)

Variables	Cut-Off	Diagnostic Values					ROC Curve			Odds Ratio		
		Sensitivity	Specificity	PPV	NPV	Accuracy	Area (SE)	95%CI	<i>p</i>	Odds Ratio	95%CI	<i>p</i>
Naples	≥4	66.7	72.4	63.6	75.0	70.0	0.690	0.536-0.843	0.023	5.25	1.551-17.767	<0.001
CONUT	≥4	61.9	89.7	81.3	76.5	78.0	0.740	0.584-0.895	0.004	14.083	3.191-62.150	<0.001
PNI	<44.95	76.0	86.2	80.0	83.3	82.0	0.792	0.650-0.935	<0.001	20	4.659-85.848	<0.001
SIS	≥2	76.2	72.4	66.7	80.8	74.0	0.755	0.617-0.892	0.002	8.4	2.306-30.603	<0.001

CONUT: Controlling Nutritional Status, PNI: Prognostic Nutritional Index, SIS: Systemic Inflammation Score

differences were identified between the two groups in terms of age or gender ($p=0.315$ and $p=0.286$, respectively). Furthermore, no differences were identified regarding the type of operation or the use of laparoscopy ($p=0.603$ and $p=0.704$, respectively). The median albumin level of 3.5 mg/dL (2.6-4.5) was observed to be significantly lower in patients who had died than in patients who were still alive (median = 4.1 mg/dL, 3.2-4.4; $p=0.001$) (Table I). There was no significant difference in cholesterol levels between the two groups ($p=0.250$). The median NLR of deceased patients was significantly higher than that of those still alive ($p=0.005$). The median LMR of the deceased patients was lower than that of patients who were still alive ($p=0.009$). There was no statistically significant difference between groups in terms of TNM stage ($p=0.053$) (Table I).

Table III Kaplan Meier Survival Analysis Results

Variables	Estimated Mean Survival Duration	Std. Error	95% Confidence Interval		Log-rank test statistical significance	
			Lower Bound	Upper Bound		
PNI	≥44.95	37.157	1.216	34.773	39.540	<0.001
	<44.95	27.179	1.654	23.936	30.421	
CONUT	<4	36.194	1.229	33.784	38.604	<0.001
	≥4	26.650	1.862	23.000	30.300	
SIS	<2	36.731	1.379	34.028	39.433	<0.001
	≥2	29.296	1.698	25.967	32.625	
Naples	<4	35.849	1.411	33.083	38.615	0.010
	≥4	29.915	1.834	26.321	33.509	
Overall Estimated Survival Duration		33,150	1.207	30.785	35.516	

CONUT: Controlling Nutritional Status, PNI: Prognostic Nutritional Index, SIS: Systemic Inflammation Score

Table IV Multivariate Cox Regression Analysis Results

Variables	B	SE	Wald	Sig.	Exp(B)	95% CI for Exp(B)	
						Lower	Upper
Albumin	-1.470	0.454	10.478	0.001	0.230	0.094	0.560
NLR	0.032	0.012	7.288	0.007	1.032	1.009	1.057
PNI	-0.111	0.033	11.275	0.001	0.895	0.838	0.955
LMR	-0.465	0.206	5.079	0.024	0.628	0.419	0.941

NLR: Neutrophil-to-Lymphocyte Ratio, LMR: Lymphocyte-to-Monocyte Ratio, PNI: Prognostic Nutritional Index

A statistical analysis of the nutritional scores of two groups revealed that the majority of deceased patients had a Naples score of 3-4 (66.67%), while the majority of the other group had a Naples score of 1-2 (65.52%). This difference was found to be statistically significant ($p=0.022$). Patients who died had a higher median CONUT score of 4 than patients who survived (median 2; $p=0.004$). Similarly, the SIS score of deceased patients was significantly higher compared to the other group ($p<0.001$). The PNI score of 49.06 ± 5 was significantly higher in living patients compared to 42.08 ± 7.29 in deceased patients ($p<0.001$).

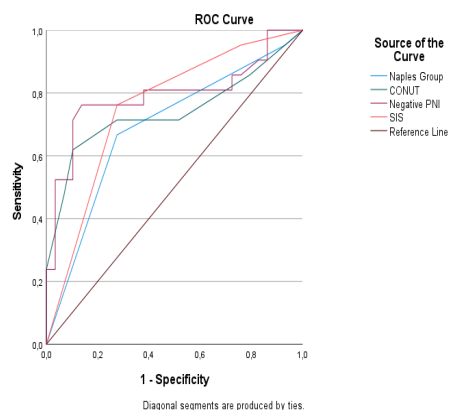


Figure I Receiver operating curve of prognostic scores in the distinction between groups

To assess the optimal values of Naples, CONUT, PNI, and SIS scores for distinguishing between alive and deceased patient groups, the area under the curve and the Youden index were employed in ROC analysis (Figure I and Table II). For the prediction of mortality, the most suitable Naples cut-off value was determined to be ≥ 4 with 66.7% sensitivity, 72.4% specificity, 63.6% positive predictive value, 75% negative predictive value, and 70% test accuracy (OR 5.25, 95% CI 1.551-17.767, $p < 0.001$). Similarly, the optimal CONUT cut-off value was also found to be ≥ 4 with 61.9% sensitivity, 89.7% specificity, 81.3% positive predictive value, 76.5% negative predictive value, and 78% test accuracy (OR 14.083, 95% CI 3.191-62.150, $p < 0.001$). The optimal PNI cut-off was < 44.95 with 76% sensitivity, 86.2% specificity, 80.0% positive predictive value, 83.3% negative predictive value, and 82% test accuracy (OR 20, 95% CI 4.659-85.848, $p < 0.001$). Lastly, the optimal SIS cut-off was ≥ 2 with 76.2% sensitivity, 72.4% specificity, 66.7% positive predictive value, 80.8% negative predictive value, and 74% test accuracy (OR 8.4, 95% CI 2.306-30.603, $p < 0.001$). Among these prognostic scores, PNI was found to be slightly better than the other scores, with a higher area under the curve and a higher odds ratio. A PNI score under 44.95 increased the likelihood of mortality by approximately 19 times. To assess the survival analysis, both Kaplan-Meier and Cox regression analyses were performed. The median survival time for all patients was 30 months. For deceased patients, the median survival time was 24 months, while for surviving patients, it was 36 months. The Kaplan-Meier survival curves indicated that higher Naples, CONUT, and SIS scores were associated with shorter survival times, while a higher PNI score was associated with longer survival (Figures IIa, IIb, IIc, IId, and Table III). The mean estimated survival duration for patients whose Naples scores were 4 or higher was 29.91 ± 1.83 months, while the mean estimated survival duration for patients with Naples scores lower than 4 was significantly higher at 35.84 ± 1.41 months ($p = 0.010$, Table III). Cox regression analysis further identified that albumin, NLR, LMR, and PNI were significant predictors of survival. Multivariate Cox regression analysis results indicated that lower albumin levels, higher NLR, lower LMR, and lower PNI scores significantly increased the

risk of mortality (Table IV and Figure III for details). These findings highlight the importance of nutritional and inflammatory status in predicting postoperative outcomes in gastric cancer surgery patients.

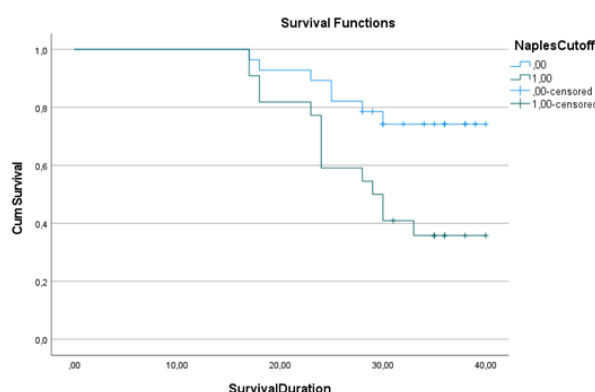


Figure IIa Kaplan Meier Survival Analysis Graph of Naples Score Cutoff

Table V Demographic specifications of the patients and comparison between the patient groups

Variables		Naples<4	Naples≥4	p value
Age		63.71±10.75	67.95±10.33	0.165
Gender	Male	22 (78.57%)	18 (81.82%)	0.776
	Female	6 (21.43%)	4 (18.18%)	
Operation Type	Subtotal	12 (42.86%)	5 (22.73%)	0.136
	Total	16 (57.14%)	17 (77.27%)	
Laparoscopic	Laparotomy	14 (50.00%)	13 (59.09%)	0.522
	Laparoscopy	14 (50.00%)	9 (40.91%)	
Albumin		4.15 (2.8-4.5)	3.61 (2.6-4.2)	<0.001
Cholesterol		192.64±45.81	152.18±32.96	0.001
NLR		2.47 (1.27-11.7)	3.97 (1.74-109.6)	0.003
LMR		3.74 (1.31-7.36)	2.35 (1.26-3.78)	0.002
Mortality	Alive	21 (75%)	8 (36.36%)	0.006
	Deceased	7 (25%)	14 (63.64%)	
CONUT		1.5 (0-10)	4 (1-9)	0.005
PNI		49.11±6.30	42.33±5.85	<0.001
SIS		1 (0-2)	2 (1-2)	<0.001
TNM	T1N0	9 (32.14%)	0 (0.00%)	0.095
	T2N0	1 (3.57%)	0 (0.00%)	
	T2N1	0 (0.00%)	1 (4.55%)	
	T3N0	4 (14.29%)	2 (9.09%)	
	T3N1	2 (7.14%)	1 (4.55%)	
	T3N2	2 (7.14%)	1 (4.55%)	
	T3N3	2 (7.14%)	8 (36.36%)	
	T4N0	1 (3.57%)	1 (4.55%)	
	T4N1	1 (3.57%)	1 (4.55%)	
	T4N2	2 (7.14%)	1 (4.55%)	
T4N3	4 (14.29%)	6 (27.27%)		

NLR: Neutrophil-to-Lymphocyte Ratio, LMR: Lymphocyte-to-Monocyte Ratio, CONUT: Controlling Nutritional Status, PNI: Prognostic Nutritional Index, SIS: Systemic Inflammation Score

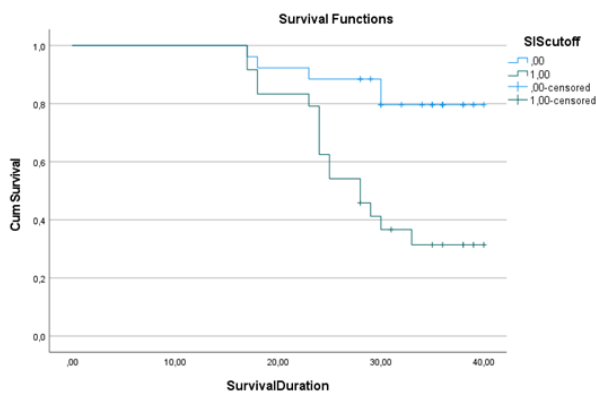


Figure IIb Kaplan Meier Survival Analysis Graph of SIS Cut-off

Further analysis was conducted by dividing patients into two groups based on the Naples score cut-off value of ≥ 4 , as determined by the Youden index. Patients with Naples scores of 4 or higher were characterized by lower albumin levels, lower cholesterol levels, higher NLR, lower LMR, higher mortality rates, higher CONUT scores, lower PNI scores, and higher SIS scores (Table V).

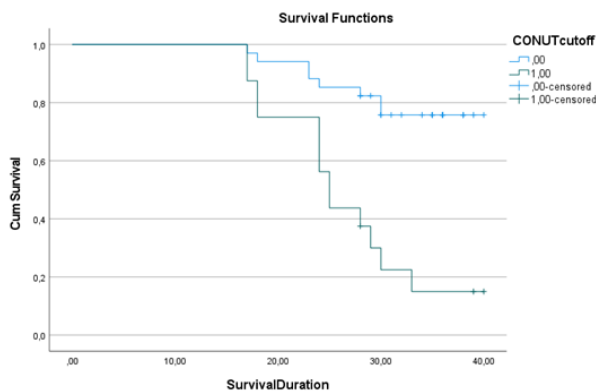


Figure IIc Kaplan Meier Survival Analysis Graph of CONUT Cutoff

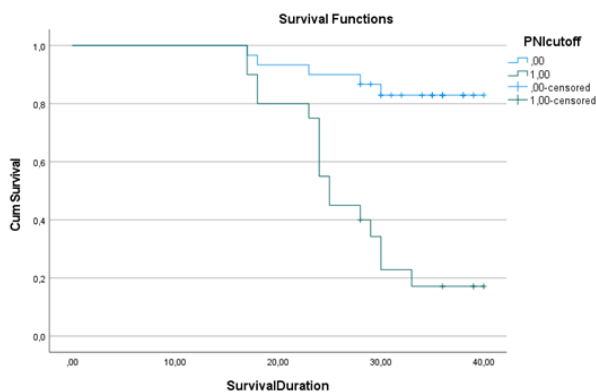


Figure II d Kaplan Meier Survival Analysis Graph of PNI Cutoff

These results further validate the importance of the NAPLES score in predicting patient outcomes.

A higher NAPLES score indicates a worse prognosis, underscoring the relevance of nutritional and inflammatory status as critical factors in the postoperative survival of gastric cancer patients. The detailed statistical analysis emphasizes that patients with higher NAPLES scores tend to have poorer survival outcomes, highlighting the utility of this score in clinical decision-making and patient management.

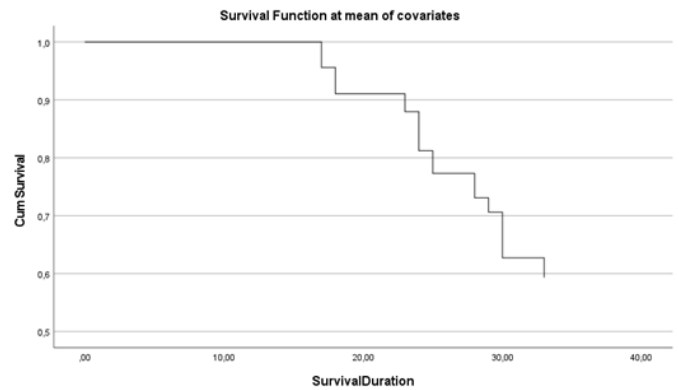


Figure III Cox Regression Analysis Graph

Discussion

This study aimed to compare the prognostic value of various nutritional and inflammatory scores in predicting mortality in patients undergoing gastric cancer surgery. Our findings revealed that Naples, CONUT, PNI and SIS scores were significantly associated with mortality and that PNI was superior to other scoring methods.

GC ranks among the leading causes of cancer-related deaths worldwide (11). The prognosis is quite poor in metastatic patients. The nutritional status of these patients is often worse due to gastrointestinal involvement and cancer-related cachexia. Impaired nutritional status and immune response are among the reasons for the short survival time in these patients (12).

In many studies, cancers have been shown to be affected by the immune response and related to nutritional status. This has led to the development of new biomarkers of the immune system and nutrition-based prognostic scoring systems (13).

The inflammatory response in the tumor may also play a role in the destruction of tumor cells and angiogenesis. The inflammatory response can

be altered by exposing tumors to radiotherapy and chemotherapy. Lymphocytes play an important role in this reaction. Lymphopenia in many tumors, including GC, is also associated with adverse effects and poor prognosis (14,15). On the other hand, increased tumoral neutrophil infiltration usually correlates with poor clinical features. Neutrophils play a role in tumor cell proliferation and tumor formation by activating cytokines and causing metastasis (16,17). Therefore, NLR and LMR have been evaluated in many studies, and increasing NLR and decreasing LMR are generally associated with worse outcomes (18).

Malnutrition is intricately linked to angiogenesis and tumor growth, thereby facilitating disease progression. Serum albumin levels serve as a crucial indicator of nutritional status and inflammatory burden, functioning as a negative acute phase reactant. Hypoalbuminemia is frequently associated with unfavorable outcomes in various malignancies (19). Our study similarly found that hypoalbuminemia correlates with poor prognosis in GC. Beyond albumin, cholesterol levels also reflect nutritional status, with low cholesterol being indicative of a poor prognosis (20). Therefore, nutritional status scores often include both albumin and cholesterol measurements.

This study shows that the NPS is an independent indicator of outcome in patients who undergo surgery for GC. By including all previously used biomarkers in the PNI, we covered both nutritional and inflammatory status. The PNI worsened with tumor progression, suggesting a strong correlation between tumor status and patient status, and was a significant predictor of long-term outcome. Its prognostic performance turned out to be much better than that of previous scoring systems and significantly improved the current prognostic model. Further analysis, based on the Naples score cut-off value of ≥ 4 , demonstrated its significant prognostic value. Patients with Naples scores ≥ 4 had a worse prognosis compared to those with scores < 4 . The median survival time for patients with Naples < 4 was 30 months, indicating better outcomes. This underscores the utility of the Naples score in clinical decision-making and highlights its importance in

risk stratification and management of gastric cancer patients.

The two indicators that make up PNI are obtained by routine peripheral blood laboratory testing before surgery. We evaluated the predictive performance of various prognostic scores using time-dependent ROC curve analysis. The findings indicated that PNI had a higher area under the curve and a greater odds ratio compared to NPS, CONUT, and SIS, making it the most effective predictor.

This study has several limitations. Firstly, as a retrospective study, it is inherently subject to potential selection bias. Secondly, the lack of external validation and the fact that it was conducted at a single center with a moderate sample size might have diminished the strength of its findings. Future prospective and multi-institutional studies are required to validate these results.

In conclusion, PNI, CONUT, SIS, and NPS, which evaluate the calculated immune nutritional status, predict GC patient outcomes. PNI appears superior to others in this respect.

References

1. Müsri FY, Mutlu H, Karaağaç M, Eryılmaz MK, Gündüz Ş, Artaç M. Primary Tumor Resection and Survival in Patients with Stage IV Gastric Cancer. *J Gastric Cancer* 2016;16:78-84.
2. Alkurt EG, Durak D, Turhan VB, Sahiner IT. Effect of C-Reactive Protein-to-Albumin Ratio on Prognosis in Gastric Cancer Patients. *Cureus* 2022;14.: e23972.
3. Sakurai K, Ohira M, Tamura T, et al. Predictive Potential of Preoperative Nutritional Status in Long-Term Outcome Projections for Patients with Gastric Cancer. *Ann Surg Oncol* 2016;23:525-533.
4. Fu X, Li T, Dai Y, Li J. Preoperative systemic inflammation score (SIS) is superior to neutrophil to lymphocyte ratio (NLR) as a predicting indicator in patients with esophageal squamous cell carcinoma. *BMC Cancer* 2019;19:721.
5. Klute KA, Brouwer J, Jhaver M, et al. Chemotherapy dose intensity predicted by baseline nutrition assessment in gastrointestinal malignancies: A multicentre analysis. *Eur J Cancer* 2016;63:189-200.
6. Nakagawa N, Yamada S, Sonohara F, et al. Clinical Implications of Naples Prognostic Score in Patients with Resected Pancreatic Cancer. *Ann Surg Oncol* 2020;27:887-895.
7. Sun F, Zhang C, Liu Z, Ai S, Guan W, Liu S. Controlling Nutritional Status (CONUT) score as a predictive marker for short-term complications following gastrectomy of gastric cancer: a retrospective study. *BMC Gastroenterol* 2021;21:107.
8. Itoh S, Tsujita E, Fukuzawa K, et al. Prognostic significance of preoperative PNI and CA19-9 for pancreatic ductal adenocarcinoma: A multi-institutional retrospective study. *Pancreatology* 2021;21:1356-1363.
9. Nomoto D, Baba Y, Akiyama T, et al. Adapted systemic inflammation score as a novel prognostic marker for esophageal squamous cell carcinoma patients. *Ann Gastroenterol Surg* 2021;5:669-676.
10. Xiong J, Hu H, Kang W, et al. Prognostic Impact of Preoperative Naples Prognostic Score in Gastric Cancer Patients Undergoing Surgery. *Front Surg* 2021;8:617744.
11. Rawla P, Barsouk A. Epidemiology of gastric cancer: global trends, risk factors and prevention. *Prz Gastroenterol* 2019;14:26-38.
12. Ramos MFKP, Pereira MA, de Castria TB, et al. Remnant gastric cancer: a neglected group with high potential for immunotherapy. *J Cancer Res Clin Oncol* 2020;146:3373-3383.
13. Zheng X, Li L, Yu C, et al. Establishment of a tumor immune microenvironment-based molecular classification system of breast cancer for immunotherapy. *Aging (Albany NY)* 2021;13:24313-24338.
14. Eberst G, Vernerey D, Laheurte C, et al. Prognostic value of CD4+ T lymphopenia in non-small cell lung Cancer. *BMC Cancer* 2022;22:529.
15. Tataru T, Suzuki S, Kanaji S, et al. Lymphopenia predicts poor prognosis in older gastric cancer patients after curative gastrectomy. *Geriatr Gerontol Int* 2019;19:1215-1219.
16. Zhu T, Zou X, Yang C, et al. Neutrophil extracellular traps promote gastric cancer metastasis by inducing epithelial mesenchymal transition. *Int J Mol Med* 2021;48:127.
17. Guan X, Lu Y, Zhu H, et al. The Crosstalk Between Cancer Cells and Neutrophils Enhances Hepatocellular Carcinoma Metastasis via Neutrophil Extracellular Traps-Associated Cathepsin G Component: A Potential Therapeutic Target. *J Hepatocell Carcinoma* 2021;8:451-465.
18. Garcea G, Ladwa N, Neal CP, Metcalfe MS, Dennison AR, Berry DP. Preoperative neutrophil-to-lymphocyte ratio (NLR) is associated with reduced disease-free survival following curative resection of pancreatic adenocarcinoma. *World J Surg* 2011;35:868-872.
19. Hardt J, Pilz L, Magdeburg J, Kienle P, Post S, Magdeburg R. Preoperative hypoalbuminemia is an independent risk factor for increased high-grade morbidity after elective rectal cancer resection. *Int J Colorectal Dis* 2017;32:1439-1446.
20. Hirano H, Ide H, Lu Y, Inoue Y, Okada H, Horie S. Impact of Pretreatment Total Cholesterol Level Is Associated With Metastasis of Prostate Cancer. *Am J Mens Health* 2020;14:1557988320918788.